EXHIBIT A

Chapter 4
ADVISORY ACTIONS

This chapter defines and establishes uniform guidance and procedures for Warning Letters and Untitled Letters.

This chapter includes the following sections:

4-1 WARNING LETTERS

4-1-1 Warning Letter Procedures

When it is consistent with the public protection responsibilities of the agency and depending on the nature of the violation, it is the Food and Drug Administration's (FDA's) practice to give individuals and firms an opportunity to take voluntary and prompt corrective action before it initiates an enforcement action. Warning Letters are issued to achieve voluntary compliance and to establish prior notice. (Prior notice is discussed in Chapter 10.) The use of Warning Letters and prior notice are based on the expectation that most individuals and firms will voluntarily comply with the law.

The agency position is that Warning Letters are issued only for violations of regulatory significance. Significant violations are those violations that may lead to enforcement action if not promptly and adequately corrected. A Warning Letter is the agency's principal means of achieving prompt voluntary compliance with the Federal Food, Drug, and Cosmetic Act (the Act).

The Warning Letter was developed to correct violations of the statutes or regulations. Also available to the agency are enforcement strategies which are based on the particular set of circumstances at hand and may include sequential or concurrent FDA enforcement actions such as recall, seizure, injunction, administrative detention, civil money penalties and/or prosecution to achieve correction. Despite the significance of the violations, there are some circumstances that may preclude the agency from taking any further enforcement action following the issuance of a Warning Letter. For example, the violation may be serious enough to warrant a Warning Letter and subsequent seizure; however, if the seizable quantity fails to meet the agency's threshold value for seizures, the agency may choose not to pursue a seizure. In this instance, the Warning Letter would document prior warning if adequate corrections are not made and if enforcement action is warranted at a later time.

Responsible officials in positions of authority in regulated firms have a legal duty to implement whatever measures are necessary to ensure that their products, practices, processes, or other activities comply with the law. Under the law such individuals are presumed to be fully aware of their responsibilities. Consequently,

responsible individuals should not assume that they would receive a Warning Letter, or other prior notice, before FDA initiates enforcement action.

FDA is under no legal obligation to warn individuals or firms that they or their products are in violation of the law before taking enforcement action, except in a few specifically defined areas. When acting under the authority of Subchapter C - Electronic Product Radiation Control (formerly the Radiation Control for Health and Safety Act of 1968) of Chapter V of the Act, FDA is required by law to provide a written notification to manufacturers when the agency discovers products that fail to comply with a performance standard or that contain a radiation safety defect. Because of the legal requirements of Subchapter C, minor variations in the procedures may occur.

A Warning Letter is informal and advisory. It communicates the agency's position on a matter, but it does not commit FDA to taking enforcement action. For these reasons, FDA does not consider Warning Letters to be final agency action on which it can be sued.

There are instances when issuing a Warning Letter is not appropriate, and, as previously stated, a Warning Letter is not a prerequisite to taking enforcement action. Examples of situations where the agency will take enforcement action without necessarily issuing a Warning Letter include:

1. The violation reflects a history of repeated or continual conduct of a similar or substantially similar nature during which time the individual and/or firm has been notified of a similar or substantially similar violation;
2. The violation is intentional or flagrant;
3. The violation presents a reasonable possibility of injury or death;
4. The violations, under Title 18 U.S.C. 1001, are intentional and willful acts that once having occurred cannot be retracted. Also, such a felony violation does not require prior notice. Therefore, Title 18 U.S.C. 1001 violations are not suitable for inclusion in Warning Letters; and,
5. When adequate notice has been given by other means and the violations have not been corrected, or are continuing. See Chapter 10, Prior Notice, for other methods of establishing prior notice.

In certain situations, the agency may also take other actions as an alternative to, or concurrently with, the issuance of a Warning Letter. For example:

1. The product is adulterated under Section 402(a)(3) or 402(a)(4) of the Act;
2. There is a violation of current good manufacturing practices (CGMP);
3. The product contains illegal pesticide residues; or
4. The product shows short contents, subpotency, or superpotency.

Additional instructions for Warning Letters in specific product areas are found in compliance program guidance and in compliance policy guides.

Also, see Exhibit 4-1, the agency's "Procedures for Clearing FDA Warning Letters and Untitled Letters." All agency components responsible for issuing Warning Letters and Untitled Letters must follow these procedures. Developed to facilitate review of all Warning Letters and Untitled Letters by the Office of Chief Counsel (OCC), the procedures provide instructions for submitting such letters to OCC, and include timeframes and routing information.

4-1-2 Warning Letters To Government Agencies

Government establishments should be held to the same standards as nongovernment establishments. The public health standards are identical; however, the method used to ensure compliance with these standards may vary. FDA believes that government establishments will achieve and maintain a higher rate of voluntary compliance with FDA regulations compared with nongovernment establishments. Efforts to obtain voluntary compliance should be made and documented before recommending the issuance of a Warning Letter. These efforts may include discussing the violations with the responsible government officials by phone or in a meeting, recommending an Untitled Letter, or requesting a written corrective action plan and periodic progress reports. The government establishment's progress should be monitored and a follow-up inspection should be scheduled within a reasonable time consistent with the noted violations to confirm correction of the violations.

Whenever significant violations are observed at a government establishment, or if attempts to achieve compliance have been ineffective, the office (or center) should arrange a meeting with OEIO, OCC, and the relevant center to determine a strategy to achieve timely and effective compliance. The meeting should include the Office of Partnerships (OP) if the government establishment is a state or local agency.

Also, see Exhibit 4-1, the agency's "Procedures for Clearing FDA Warning Letters and Untitled Letters." All agency components responsible for issuing Warning Letters and Untitled Letters must follow these procedures.

4-1-3 Issuing Warning Letters - Factors to Consider

The Warning Letter is the agency's principal means of notifying regulated industry of violations and achieving prompt voluntary correction. Warning Letters can be issued at the discretion of the program office director without center concurrence, except in specific program areas that require prior center concurrence. Warning Letters may also be generated through work done at agency headquarters (ORA or centers), processed under appropriate procedures and issued under the authority of a division or office director. (See Center Concurrence and Letters Issued by centers. Also, see Exhibit 4-1, the agency's "Procedures for Clearing FDA Warning Letters and Untitled Letters." All agency components responsible for issuing Warning Letters and Untitled Letters must follow these procedures.)

1. General Considerations:

   In determining whether to issue a Warning Letter, program office directors and center or other officials with authority to issue should consider whether:

   a. Evidence shows that a firm, product, and/or individual is in violation of the law or regulations and that failure to achieve adequate and prompt correction may result in agency consideration of an enforcement action;

   b. The violation(s) are determined to be of regulatory significance, and the issuance of a Warning Letter is appropriate and consistent with agency policy, as described in Compliance Policy Guides or elsewhere; and,

   c. There is a reasonable expectation that the responsible firm and persons will take prompt corrective action.

2. Ongoing or Promised Corrective Actions

   Corrective action may be undertaken or promised during an establishment inspection or addressed in correspondence to the agency after an inspection. Ongoing or promised corrective actions generally do not preclude the issuance of a Warning Letter. In addition to being the agency's primary means to achieve prompt, voluntary compliance, Warning Letters remain a primary means to establish prior notice (see Chapter 10) and serve to ensure that the seriousness and scope of the observed violations are understood by top management and that the appropriate resources are allocated to fully correct the violations and to prevent recurrence.

When a firm is in the process of correcting the violations or has made a written promise to take prompt corrective action, a program office or center should consider the following factors when determining whether or not to issue a Warning Letter:

a. The firm's compliance history, e.g., a history of serious violations, or failure to prevent the recurrence of violations;

b. The nature of the violation, e.g., a violation that the firm was aware of (was evident or discovered) but failed to correct;

c. The risk associated with the product and the impact of the violations on such risk;

d. The overall adequacy of the firm's corrective action and whether the corrective action addresses the specific violations, related violations, related products or facilities, and contains provisions for monitoring and review to ensure effectiveness and prevent recurrence;

e. Whether documentation of the corrective action was provided to enable the agency to undertake an informed evaluation;

f. Whether the timeframe for the corrective action is appropriate and whether actual progress has been made in accordance with the timeframe; and,

g. Whether the corrective action taken ensures sustained compliance with the law or regulations. In the case of Warning Letters being considered for products offered for sale through internet web sites, corrective action to remove claims from or inactivate the website is easily reversible, and should be carefully considered, along with the other factors above, in determining whether or not to issue a Warning Letter. Warning Letters for, or involving, internet web sites should be issued in as close proximity as possible to the time when the claims were last observed, and reference to the date on which the claims were observed should be included in the letter.

If a decision is made not to issue a Warning Letter, see "Response Letter" below. Relying on a firm's promised corrective actions does not preclude consideration of regulatory action should we later observe that the same or similar violations have not been corrected.

3. Completed Corrective Actions

As a general rule, a Warning Letter should not be issued if the agency concludes that a firm's corrective actions are adequate and that the violations that would have supported the letter have been corrected. If you believe that an exception is necessary due to the

facts or circumstances of the case (e.g., the firm's compliance history, the nature of the violation, or the risk associated with the product) discuss this background in the Warning Letter referral package and be sure to adapt the language in the proposed letter to fit the circumstances (e.g., recite the history and the consequences if there is a recurrence).

If a decision is made not to issue a Warning Letter, see "Response Letter" below. Relying on a firm's completed corrective actions does not preclude consideration of regulatory action should we later observe that the same or similar violations have not been corrected.

4. Response Letter

If a decision is made to not issue a Warning Letter because adequate corrective action has been taken, or because corrective action is being taken or has been promised, it is recommended that an alternative form of communication (e.g., a response letter to the firm's letter promising corrective action) be issued to the responsible individuals at the firm to supplement the record of the violation(s) and reflect the agency's decision to rely on the firm's actions and/or promises. The response letter should indicate that the agency is relying on the firm's corrections or commitment regarding corrective actions. Further, the letter may include a statement that should we later observe that these or similar violations have not been corrected; regulatory action (e.g., seizure, injunction and, if appropriate, civil penalties) may be taken without further notice.

5. Verification of Corrective Actions

Verification of the overall completeness and effectiveness of the corrective action should be undertaken during the next inspection, the timing of which may be expedited or routine as determined by the issuing office.